

$(-11, 32)^\perp$

Application No.: 09/913,419

2

Docket No.: 03991/000J678-USO

AMENDMENTS TO THE CLAIMS

1. (currently amended) An isolated cytokine-binding domain of Domain 4 of a β_c chain or ~~analogous structure of a cytokine receptor, or portion thereof,~~ which binds to at least one cytokine and is capable of transducing a cytokine signal through a single cytokine receptor, said domain ~~comprising a portion of the B'-C' loop of the cytokine-binding domain~~ comprising a region defined by an N-terminus of Domain 4 and by a B'-C' loop, said B'-C' loop (including residues Tyr365, His367, and Ile368 of Domain 4 of the β_c chain.
2. (currently amended) The ~~eytokine-binding~~ cytokine-binding domain according to claim 1 comprising ~~a portion of the B'-C' loop of domain Domain 4 and a groove which is defined by the B'-C', F'-G' loops, and wherein the F'-G' loop comprises residues 418 and 421 of Domain 4 of the β_c chain,~~ and the N-terminal section of Domain 4.
3. (currently amended) The ~~eytokine-binding~~ cytokine-binding domain according to claim 1 further including a Tyrosine residue capable of interaction with an α chain subunit or with Domain 3 of the β β_c chain subunit to allow high affinity binding of the cytokine.
4. (currently amended) The ~~eytokine-binding~~ cytokine-binding domain according to claim 3 wherein the tyrosine is Tyr421 ~~or equivalent residue of an analogous common signalling structure.~~
5. (currently amended) The ~~eytokine-binding~~ cytokine-binding domain according to claim 1 wherein the B'-C' loop residues of Domain 4 of the β_c chain ~~comprises residues 365 to 368 forming a type 1 β -turn or an analogous structure in an analogous common signalling structure.~~
6. (currently amended) The ~~eytokine-binding~~ cytokine-binding domain according to claim 1 wherein the binding domain of the β_c chain, ~~or portion thereof~~ which binds to at least one cytokine, is defined by an area bordered by any one of the following residues (including Lys362, Tyr365, His367, Ile368, Arg418, Gly420, Asn422, Thr416, Ile338, Gln339, Met340 and Met361 ~~or equivalent residues in an analogous common signalling structure of a cytokine receptor.~~

{W:\03991\000j678us0\00420763.DOC [REDACTED]}

Application No.: 09/913,419

3

Docket No.: 03991/000J678-US0

7. (canceled)

8. (currently amended) The ~~cytokine-binding~~ cytokine-binding domain according to claim 1 that binds to at least two cytokines selected from the group consisting of IL-3, IL-5, GM-CSF, IL-4 and IL-13.

9. (canceled)

10. (currently amended) The ~~cytokine-binding~~ cytokine-binding domain according to ~~claim 9~~ claim 1 wherein the ~~common~~- β_c chain is derived from a receptor selected from the group consisting of IL-5 receptor, IL-3 receptor and GM-CSF receptor.

11. (currently amended) The ~~cytokine-binding~~ cytokine-binding domain according to claim 2 wherein the F'-G' loop adopts a type IV β turn at its tip in ~~Domain 4 and includes the residues Arg418 and Tyr421.~~

12. (currently amended) A method of identifying a compound having cytokine agonist or antagonist activity which comprises:

subjecting a potential cytokine agonist and/or cytokine antagonist compound to the cytokine binding domain or portion thereof according to claim 1; and

determining the presence of an agonist or antagonist response to the compound on the activity of a cytokine.

13. (currently amended) A method of identifying a compound having a cytokine agonist or
antagonist activity, which comprises:

subjecting a potential cytokine antagonist to the cytokine binding domain or portion thereof according to claim 1; and

{W:\03991\000j678us0\00420763.DOC 11/11/2001 11:11:11 AM}

Application No.: 09/913,419

4

Docket No.: 03991/000J678-US0

identifying a compound that has bound to the cytokine-binding domain wherein said compound has an agonist or antagonist response on the activity of the cytokine.

14. (currently amended) A The method according to claim 12 wherein the cytokine is selected from the group consisting of IL-3, IL-5, GM-CSF, IL-4 and IL-13; and the presence of an agonist or antagonist is determined by the ability of the agonist or antagonist to activate or inhibit an IL-3, IL-5, GM-CSF, IL-4, or IL-13 response.

15. (currently amended) A The method according to claim 12 wherein the cytokine agonist or antagonist further binds to Tyr421 ~~or an equivalent residue of a common signalling unit of a~~ cytokine receptor.


16. (previously presented) A cytokine agonist or antagonist identified by a method according to claim 12.

17. (previously presented) An antibody or fragment thereof to the cytokine binding domain according to claim 1.

18. (currently amended) The cytokine binding domain according to claim 1 comprising a mutation directed to ~~any one of the residues~~ a residue selected from ~~the a group including consisting of Gln340, Ile338 and Met361 or an equivalent residue of a common signalling unit of a cytokine receptor of Domain 4 of the β_c chain.~~

19. (original) A method of preventing or treating a cytokine-related condition, which method comprises administering to a subject an effective amount of an agonist or antagonist according to claim 16.

20. (original) A method of preventing or treating a cytokine-related condition, which method comprises administering to a subject an effective amount of an antibody according to claim 17.

{W:\03991\000j678us0\00420763.DOC  }

Application No.: 09/913,419

5

Docket No.: 03991/000J678-US0

21. (currently amended) The method according to claim 19 wherein the cytokine-related condition is selected from the group including survival or activation of eosinophil function, asthma, leukemia, breast cancer, prostate cancer, small cell lung carcinoma, colon cancer, chronic inflammation including rheumatoid arthritis, immunosuppression, allergy, lymphoma, and cachexia, and wherein said cytokine agonist or antagonist is an antagonist.

22. (previously presented) The method according to claim 20 wherein the cytokine-related condition is selected from the group including survival or activation of eosinophil function, asthma, leukemia, breast cancer, prostate cancer, small cell lung carcinoma, colon cancer, chronic inflammation including rheumatoid arthritis, immunosuppression, allergy, lymphoma, and cachexia.


23. (currently amended) The method according to claim 19 wherein the cytokine-related condition is allergic inflammation and the antagonist inhibits the binding of ~~any one~~ of IL-5, IL-3 or GM-CSF to the IL-5, IL-3 or GM-CSF receptor.

24. (currently amended) The method according to claim 20 wherein the cytokine-related condition is allergic inflammation and the ~~antagonist~~ antibody inhibits the binding of any one of IL-5, IL-3 or GM-CSF to the IL-5, IL-3 or GM-CSF receptor.

25. (previously presented) The method according to claim 23 wherein the allergic inflammation results in asthma.

26. (previously presented) The method according to claim 24 wherein the allergic inflammation results in asthma.

27. (previously presented) The method according to claim 19 wherein the cytokine-related condition is selected from the group including hemopoiesis, boosting immune response, suppression of embryonic stem cell differentiation, immunostimulation, antitumor activity, expansion of early

{W:\03991\000j678us0\00420763.DOC  }

Application No.: 09/913,419

6

Docket No.: 03991/000J678-USO

hemopoietic cells, anemia, correcting thrombocytopenia, wherein said cytokine agonist or antagonist is an agonist.

28. (previously presented) The method according to claim 13 wherein the cytokine is selected from the group consisting of IL-3, IL-5, GM-CSF, IL-4 and IL-13; and the presence of an agonist or antagonist is determined by the ability of the agonist or antagonist to activate or inhibit an IL-3, IL-5 GM-CSF, IL-4, or IL-13 response.

29. (currently amended) The method according to claim 13 wherein the cytokine agonist or antagonist further binds to Tyr421 or an equivalent residue of a common signalling signaling unit of a cytokine receptor.

30. (previously presented) A cytokine agonist or antagonist identified by a method according to claim 13.

31. (new) The method according to claim 13 wherein the cytokine is selected from the group consisting of IL-3, IL-5, GM-CSF, IL-4 and IL-13; and the presence of an agonist or antagonist is determined by the ability of the agonist or antagonist to activate or inhibit an IL-3, IL-5, GM-CSF, IL-4, or IL-13 response.

32. (new) The cytokine-binding domain according to claim 1 which comprises a hydrophobic patch, said patch having residues selected from a group consisting of Ile338, Ala341, Met361, and Tyr365 of Domain 4 of the β_c chain.

33. (new) The cytokine-binding domain according to claim 31 comprising Met340 and Pro342 of the β_c chain.

34. (new) The cytokine-binding domain according to claim 31 comprising Ile368 or Tyr421 of the β_c chain.

{W:\03991\000j678us0\00420763.DOC [REDACTED]}

Application No.: 09/913,419

7

Docket No.: 03991/000J678-US0

35. (new) The cytokine-binding domain according to claim 13 comprising Ile368 or Tyr421 of the β_c chain.

{W:\03991\000j678us0\00420763.DOC 2003/04/23 14:00:00}